

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>ABL - 008 - PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/BE 03/00190</b>	International filing date (day/month/year) <b>07/11/2003</b>	(Earliest) Priority Date (day/month/year) <b>08/11/2002</b>
Applicant  <b>ABLYNX N.V.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**CAMELIDAE ANTIBODIES AGAINST IMMINOGLOBULIN E AND USE THEREOF FOR THE TREATMENT OF ALLERGIC DISORDERS**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1  
☐ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 03/00190

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/42 C07K16/24 C07K16/30 C07K16/12 C07K16/10  
 C07K16/40 C07K16/28 C12N15/13 A61K39/395 A61P11/06  
 A61P35/00 A61P31/06 A61P31/16

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE, GENSEQ, EMBL

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X 01 Y	EP 0 589 840 A (CIBA GEIGY AG ;TANOX BIOSYSTEMS INC (US)) 30 March 1994 (1994-03-30) page 5, lines 4-16	1,6-24, 33,34  1-24,33, 34,58-63
X 02 Y	US 2002/054878 A1 (LOWE JOHN ET AL) 9 May 2002 (2002-05-09) claims 8-31 examples 2-4	1,6-24, 33,34  1-24,33, 34,58-63
X 03 Y	WO 91/02078 A (PEPTIDE TECHNOLOGY LTD) 21 February 1991 (1991-02-21) page 4, lines 15-24	11-25, 59,60,63  11-25, 58,61
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance  
 \*E\* earlier document but published on or after the international filing date  
 \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 \*O\* document referring to an oral disclosure, use, exhibition or other means  
 \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
 \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
 \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  
 \*&\* document member of the same patent family

Date of the actual completion of the international search

17 June 2004

Date of mailing of the international search report

01.07.2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00190

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y D4	MUYLDERMANS S: "SINGLE DOMAIN CAMEL ANTIBODIES: CURRENT STATUS" REVIEWS IN MOLECULAR BIOTECHNOLOGY, ELSEVIER, AMSTERDAM,, NL, vol. 74, no. 4, June 2001 (2001-06), pages 277-302, XP001057480 ISSN: 1389-0352 table 1	1-24, 33, 34, 58-63
Y D5	VALLE E ET AL: "Infliximab" EXPERT OPINION ON PHARMACOTHERAPY, ASHLEY, LONDON,, GB, vol. 2, June 2001 (2001-06), pages 1015-1025, XP002965315 ISSN: 1465-6566 the whole document	11-25

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-24 and 58-63 (in part) and 33, 34 (complete)

A camelidae VHH single domain antibody directed against IgE, in particular, the polypeptides represented by any of SEQ ID NO:1-11; a nucleic acid encoding for said VHH, use of the antibody for the preparation of a medicament for treating or alleviating disorders relating to inflammatory regions, a method for delivering an anti-target compound to a subject by administering the anti-IgE VHH antibodies, the anti-IgE antibodies for use in the treatment of an allergic response, the camelidae VHH anti-IgE which is humanised and the camelidae VHH anti-IgE in a composition together with a pharmaceutical carrier.

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2. claims: 11-24 and 58-63 (in part) and 25-26 (complete)

As invention 1 but relating to an anti-TNF-alpha camelidae VHH antibody (SEQ ID NO:12-14) and the uses thereof for the treatment of inflammation.

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3. claims: 11-24 a

As invention 1 but relating to an anti-CEA camelidae VHH antibody and the uses thereof for the treatment of colon cancer.

- 7 (complete)

anti-CEA camelidae VHH antibody and the uses thereof for the treatment of colon cancer.

4. claims: 11-24 a

As invention 1 but relating to a single domain antibody directed an internalising cellular receptor, in particular the anti-EGF receptor camelidae VHH antibody (SEQ ID NO:23-44) and the uses thereof for the treatment of head, neck, lung and colon cancer.

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5. claims: 11-24, 39 and 58-63 (in part) and 30 (complete)

As invention 1 but relating to single domain antibodies against an antigen of Helicobacter pylori and the uses thereof for the treatment of indigestion and gastritis.

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6. claims: 11-24, 39 and 58-63 (in part) and 31 (complete)

As invention 1 but relating to single domain antibodies against an antigen of Mycobacterium tuberculosis and the uses thereof for the treatment of tuberculosis.

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## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 11-24, 39 and 58-63 (in part) and 32 (complete)

As invention 1 but relating to single domain antibodies against an antigen of the influenza virus and the uses thereof for the treatment of flu.

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8. claims: 11-24 and 58-63 (in part) and 35-36 (complete)

As invention 1 but relating to an anti-MMP camelidae VHH antibody (SEQ ID NO:15-22) and the uses thereof for the treatment of cancer.

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9. claims: 11-24 and 58-63 (in part) and 37-38 (complete)

As invention 1 but relating to an anti-IFN-gamma camelidae VHH antibody (SEQ ID NO:45-70) and the uses thereof for the treatment of cancer, transplant rejection and an auto immune disorder.

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10. claims: 11-24 and 58-63 (in part) and 45, 46 (complete)

As invention 1 but relating to an anti-PDK camelidae VHH antibody and the uses thereof for the treatment of cancer.

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11. claims: 11-24 and 58-63 (in part) and 47, 48 (complete)

As invention 1 but relating to single domain antibodies against GSK1, Bad, caspase and Forkhead and the uses thereof for the treatment of cancer.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 03/00190

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0589840	A	30-03-1994	AT 264388 T 15-04-2004
			AU 675449 B2 06-02-1997
			AU 4748893 A 31-03-1994
			CA 2106719 A1 25-03-1994
			CN 1428352 A 09-07-2003
			CN 1088986 A , B 06-07-1994
			DE 69333484 D1 19-05-2004
			EP 0589840 A1 30-03-1994
			FI 934145 A 25-03-1994
			FI 20040696 A 19-05-2004
			JP 6225788 A 16-08-1994
			MX 9305920 A1 31-05-1994
			NO 933394 A 25-03-1994
			NZ 248743 A 27-04-1995
			SG 49856 A1 19-03-2002
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US 2002054878	A1	09-05-2002	US 6290957 B1 18-09-2001
			US 5994511 A 30-11-1999
			US 2003149244 A1 07-08-2003
			AT 253116 T 15-11-2003
			AU 741115 B2 22-11-2001
			AU 8270198 A 25-01-1999
			CA 2295540 A1 14-01-1999
			CN 1268176 T 27-09-2000
			DE 69819332 D1 04-12-2003
			DK 996728 T3 23-02-2004
			EP 0996728 A2 03-05-2000
			HU 0002474 A2 28-10-2000
			JP 2002510211 T 02-04-2002
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			PL 338030 A1 25-09-2000
			PT 996728 T 31-03-2004
			SK 187599 A3 06-08-2001
			TR 200000206 T2 21-07-2000
			WO 9901556 A2 14-01-1999
			ZA 9805500 A 24-12-1999
WO 9102078	A	21-02-1991	AU 640400 B2 26-08-1993
			AU 6145490 A 11-03-1991
			WO 9102078 A1 21-02-1991
			EP 0486526 A1 27-05-1992
			CA 2064915 A1 08-02-1991
			DE 69027121 D1 27-06-1996
			DE 69027121 T2 14-11-1996
			DK 486526 T3 24-06-1996
			JP 3443119 B2 02-09-2003
			JP 2003096096 A 03-04-2003
			JP 2003231699 A 19-08-2003
			US 2003162948 A1 28-08-2003
			US 2003232970 A1 18-12-2003
			US 2004002588 A1 01-01-2004
			US 2003171553 A1 11-09-2003
			US 2003166874 A1 04-09-2003

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 03/00190

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9102078 A		US 2003216552 A1	20-11-2003
		US 2004002589 A1	01-01-2004
		US 2003208047 A1	06-11-2003
		US 5644034 A	01-07-1997
		US 2003171554 A1	11-09-2003
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		US 2004092721 A1	13-05-2004
		US 2003225254 A1	04-12-2003
		US 6416757 B1	09-07-2002
		US 2003232971 A1	18-12-2003
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		US 2001018508 A1	30-08-2001

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/BE 03/00190

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 11-18, 25-39 and 49-57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
  
1-24 and 58-63 (in part) and 25-26, 33, 34 (complete)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 11-18, 25-39 and 49-57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.